FORM PTO-1390 (REV. 11-2000) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY 'S DOCKET NUMBER: 64251-010

U.S APPLICATION NO. (If known, see 37 CFR 1 5): 09/720190

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/DE99/00975	30 March 1999 (30.03.99)	20 June 1998 (20.06.98)

TITLE OF INVENTION: PROCESS FOR PRODUCING A POLYVINYL ALCOHOL GEL AND A MECHANICALLY HIGHLY STABLE GEL PRODUCED THEREBY

APPLICANT(S) FOR DO/EO/US: VORLOP, Klaus-Dieter and JEKEL, Maren

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [ ] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [X] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [X] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [X] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [X] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [X] An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [X] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [X] Other items or information: Acknowledgment Card
    Note that the title of the PCT Application reads: PROCESS FOR PREPARING A POLYVINYL ALCOHOL GEL AND MECHANICALLY HIGHLY STABLE GEL PRODUCED BY THIS PROCESS

"Express mail" mailing label number EK419922974US Date of Deposit 20 December 2000

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box PCT, Assistant Commissioner for Patents, Washington, DC 20231.

Meridith L. Deverman

Meridith L. Deverman

U.S. APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/720190	PCT/DE99/00975	64251-010

21. [X] The following fees are submitted:	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1000.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$860.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$710.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$690.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 860.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	24 - 20 =	4	x **$18.00**	$ 72.00	
Independent claims	1 - 3 =	0	x **$80.00**	$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$270.00**	$	
TOTAL OF ABOVE CALCULATIONS =				$ 932.00	
[ ] Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.			+	$	
SUBTOTAL =				$ 932.00	
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$	
TOTAL NATIONAL FEE =				$ 932.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$	
TOTAL FEES ENCLOSED =				$ 932.00	
				Amount to be refunded:	$
				charged:	$

a. [X] A check in the amount of $ 932.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 08-3460. A duplicate copy of this sheet is enclosed.

d. [ ] Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Robert E. Muir
Husch & Eppenberger, LLC
401 Main Street, Suite 1400
Peoria, IL 61602-1241

SIGNATURE

Robert E. Muir, Esq.
NAME

23,017
REGISTRATION NUMBER

Process for producing a polyvinyl alcohol gel and a mechanically highly stable gel produced according to the process

The invention refers to a process for producing a polyvinyl alcohol gel. The invention also refers to a mechanically highly stable gel produced according to the process.

It is well known that solutions containing polyvinyl alcohol (PVA) become more viscous when left to stand. It is also well known that PVA solutions can be converted into a gel if the solution is frozen and subsequently thawed (FR 2 107 711 A). However, gels formed in this manner have a relatively low strength.

It is also known through EP 0 107 055 B1 that the strength of PVA gels produced by freezing is increased by carrying out the freezing and thawing process at least once, but preferably repeating it two to five times. To this end, a PVA solution with a degree of saponification of $\geq$ 95 mol %, but preferably of 98 mol %, is used. The upper temperature limit for freezing the solution is –3 degrees Celsius, the cooling rate can be between 0.1 to 50 degrees Celsius per minute, the thawing rate between 0.1 to 50 degrees Celsius per minute. The PVA that is used must have a degree of polymerization of at least 700. The concentration of PVA in the solution should be over 6 wt.% and is preferably between 6 and 25 wt.%. The PVA gel produced by repeated freezing and thawing has a good mechanical strength and a high water content, which is maintained even under mechanical stress. The gel produced in this manner is highly elastic, non-toxic, and can be used in many applications, particularly in medicine.

Various substances and materials can be added to the gel to increase the strength, for instance glycol, glycerine, saccharose, glucose, agar, gelatine, methyl cellulose, etc. The admixture of agents such as heparin permits medical applications in which the active agent is continuously and evenly released from the gel over a period of time. In addition, microorganisms and enzymes can be mixed with the gel in order to create a biologically active system.

It is known from US-PS 4 663 358 that adding organic solvents to the aqueous polyvinyl solution lowers the freezing point of the solution. This prevents the water from freezing at gelling temperatures below -10 degrees Celsius, preferably approximately -20 degrees Celsius, thus forming a more homogeneous and transparent gel. The low gelling temperature is used for creating compact grained gels with sufficient mechanical strength.

Producing PVA gels using the freezing method is complicated and time consuming.

DE 43 27 923 C2 disclosed a process by which PVA gels can be produced without using the freezing process. By using a PVA solution with a degree of hydrolysis of $\geq$ 99 mol % and adding a dissolved additive that has non-aqueous OH or NH_2 groups, a gelling of the PVA can be achieved at temperatures above 0 degrees Celsius. However, the gelling process takes several hours or may even require an additional storage period of many hours in order to ensure that it is cured sufficiently to provide full strength to the gel substance. Due the nature of this method, it is disadvantageous for producing large amounts of the gel substance.

Therefore, the purpose of the present invention is to be able to produce the PVA gel substances simply and quickly, as well as improving the quality of the gel substance as much as possible in this process.

Based on this objective, the process for producing a polyvinyl alcohol gel includes the following steps:

a) Use of an aqueous polyvinyl alcohol solution with a degree of hydrolysis of $\geq$ 98 mol %.

b) The addition of an additive that is dissolved in the aqueous polyvinyl alcohol solution and forms a separate, finely distributed and aqueous phase after concentration of the solution.

c) Dehydration of the aqueous solution to a maximum residual water content of 50 wt.% in order to cause the phases to separate and hence the polyvinyl alcohol to gel.

d) Rehydration of the polyvinyl alcohol in an aqueous medium.

Surprisingly, the process according to the invention permits the gelling of the polyvinyl alcohol within several minutes at room temperature or even higher temperatures. The addition of the water-soluble additive and concentration by evaporation of the water results in a finely distributed phase separation, whereby gelling happens within a very short period of time during the PVA phase. A prerequisite is that the water-soluble additive creates a hydrous phase , so that within a very short period of time a respective proportion of water is removed through the phase separation of the PVA phase, whereby a gelling of the polyvinyl alcohol is achieved. It is advantageous if the water-soluble additive has an affinity to water at least comparable to that of the PVA.

The PVA phase, which is under-supplied with water during the gelling process, subsequently absorbs water during rehydration, whereby the elasticity and mechanical strength of the PVA gel is improved without reversing the gelling. It has been shown that a certain amount of electrolytes in the aqueous rehydration medium results in a higher stability of the PVA gel, so that the rehydration is advantageously carried out in tap water or, better yet, in a saline solution.

The process according to the invention has the advantage that it permits the production of PVA gel within a very short time without using complicated processes, in particular without a freezing process and without repeated dehydration processes, so that an extremely economical production of PVA gel is possible. The gel substances according to the invention are also characterized by a high elasticity and stability, in particular tensile strength, and in this regard are significantly superior to the PVA gel substances produced in the traditional way.

The stability and elasticity of the PVA gel substances are further enhanced by using a resaponified aqueous PVA solution in the production process.

Polyethylene glycol is a preferred water-soluble additive which is added at a concentration of 4 to 30 wt.%, preferably at 4 to 20 wt.%, and more specifically at 6 to 16 wt.%. Cellulose esters, cellulose ethers, starch esters, starch ethers, polyalkylene glycol ethers, polyalkylene glycols, long-chain alkanoles ($C_nH_{2n+1}OH$ where $n \geq 8$), sugar esters and sugar ethers are other examples of possible additives.

A particularly advantageous area of application of the PVA gel substances is their production as biologically, physically or chemically active substances, i.e. incorporating biologically, physically or chemically active material in the PVA gel. Thus the PVA gel is superbly suited for the production of chemical or biological catalysts, for instance.

The dehydration of the aqueous solution for the purpose of phase separation and the associated gelling is carried out until a maximum residual water content of 50 wt.% is reached. A lower limit for the residual water content is 10 wt.% because the PVA gel produced should be completely rehydrateable, because the elasticity of the gel substance is lower if the residual water content drops below approximately 10 wt.%, and because any incorporated biological materials can be damaged if the aforementioned residual water content is lower. An advantageous range for the residual water content is between 10 and 30 wt.%.

Dehydration can conveniently be carried out in a short period of time by evaporating water at ambient air temperature if the aqueous solution is divided into small portions, especially portions in which there is only a small proportion of starch in the solution. In particular, it is advantageous to drip the solution onto a hard surface in such a way that the diameter of the drop is at least twice that of the height of the drop. This can similarly be achieved by pouring the solution into a form and/or coating a base material. A thin, or even film-like shape permits evaporation to the required residual water content within several minutes, for instance within 15 minutes. An acceleration of the dehydration process (and, therefore, the gelling process) can be achieved by carrying out dehydration in a drying oven at a higher temperature.

The saline solution used advantageously for rehydration preferably contains polyvalent anions.

The process according to the invention is particularly advantageous for immobilizing biologically active material in that it is extraordinarily gentle on the biological material so that the biological material has a significantly higher initial activity in comparison with other immobilization processes.

This can be enhanced if the aqueous medium in which the PVA gel is rehydrated is also a culture solution for the biologically active material.

The density of the PVA gel produced according to the invention can be modified by using suitable additives. For instance, the specific gravity can be increased by adding titanium oxide and lowered by adding hollow glass microballs.

As already mentioned, gelling according to the invention is possible at room temperature but can also be carried out at lower or higher temperatures. The biologically active material that is incorporated into the PVA gel can be enzymes, microorganisms, spores and cells.

The process according to the invention can be implemented in various embodiments. For instance, it is possible to carry out the dehydration of a drop for phase creation during the falling process in a drop tower, so that when the drop impacts the surface, the gelling has already occurred after the phase separation. This production process is particularly suited for producing PVA gel substances as chromatography material whose diameter is 10 to 100 µm for laboratory purposes, and which can otherwise be between 100 and 800 µm. It is also possible to dehydrate an initial liquid that is set to a higher viscosity during extrusion of a strand and to carry out the gelling simultaneously.

Compared to previously known gel substances, the gel substance produced by the process

according to the invention has superior mechanical stability, in particular with regard to abrasion resistance and tensile strength.

These superior mechanical characteristics permit, in particular, to produce the gel substance according to the invention in a lenticular form that is advantageous to the kinetics of the reaction and in which previously known gel substances had insufficient mechanical stability, in particular agitation stability. On the other hand, the gel substance according to the invention is stable and abrasion resistant for many months, even when subject to high-speed agitation. The lenticular form with a large diameter and low height has the effect that the chemically, physically and biologically active material is always arranged near the surface, resulting in a constellation that is advantageous for the kinetics of the reaction.

The present invention permits the addition of a magnetic additive to the polyvinyl alcohol substance by a very simple method in order to collect the gel substance out of a liquid by means of magnets.

It has been shown that the pore structure of the polyvinyl alcohol gel substance can be controlled by the molecular weight of the additive that effects the phase separation. By varying the molecular weight of the added polyethylene glycol, whose molecular weight is preferably in the range of 800 and 1350, the pore size of the polyvinyl alcohol gel substance can be adjusted to between 1 and 15 μm.

Regarding the production of the aqueous solution of polyvinyl alcohol and the additive, it has been shown that the use of distilled water requires a higher degree of dehydration in order to achieve the same mechanical characteristics. The results are immediately better if normal tap water with a certain degree of hardness is used. Therefore, it can be assumed that a certain salt content in the water is advantageous for the process according to the invention.

The invention is explained in more detail below by means of examples of embodiments.

Example 1:

16.8 g of water are added to 2 g of PVA and 1.2 g of polyethylene glycol (PEG 1000). The solution is heated to 90 degrees Celsius until all the components have dissolved completely, so that a viscous, colourless solution is obtained. After cooling to 30 degrees Celsius, the polymer solution is dripped onto a polypropylene plate by means of a syringe and application of pressure. The dripping is carried out by touching the cannula onto the PP plate at a rate of approx. 1-2/second; the drop has a diameter of approx. 3 mm and a height of approx. 1 mm. After application of the drops, a white, wax-like film forms on the surface of the drops. After 89 wt.% of the water has evaporated at room temperature, the gel substances are rehydrated in water or a saline medium. The gel substances obtained have a diameter of 3-4 mm and a height of approx. 200-400 µm.

Example 2:

After the polymer suspension (composition: 2 g PVA, 1.2 g PEG 1000 and 15.8 g water) has cooled, 1 ml of a nitrogen-fixing mixed culture (Nitrosomonas europaea and Nitrobacter winogradsky) is added to 20 g of a polymer solution and dispersed, resulting in a dry biomass load of 0.06 wt.%. The production of the gel substances is carried out according to Example 1. The gel substances obtained are rehydrated in a standard mineral salt medium for nitrogen-fixers. Compared to the same amount of free nitrogen fixers, after immobilization the immobilizates produced in this way have an initial activity of approx. 70% for Nitrosomonas spp. and 100% for Nitrobacter spp.

After occlusion of the nitrogen fixers in the PVA kyrogels at –20 degrees Celsius, the initial activity of Nitrosomonas spp. is approx. 1%, at –10 degrees Celsius approx. 25% with decreasing stability of the PVA hydrogels.

The incubation of the immobilizates is carried out in the same medium at 30 degrees Celsius. After 19 days a maximum ammonium decomposition rate of between 7 and 8

µmol NH_4^+/ (g_{cat} x min) is achieved if 10 mg of gel substance is incubated in 30 ml of standard mineral salt medium.

Example 3:

1.6 g of polyethylene glycol (PEG 1000) is dissolved in 12.8 g H_2O, followed by 1.6 g of PVA. The process is continued according to Example 1. After the polymer solution has cooled to 30 degrees Celsius, 4 ml of a culture of the strictly anaerobic bacteria Clostridium butyricum NRRL B-1024, which converts glycerine into 1.3-propane diol (PD), grown overnight in an oxygen-free atmosphere is dispersed in the solution (cell load of the polymer solution: 6 x 10^7 per ml). The gel substances are produced according to Example 1. After 70 wt.% of the water has evaporated at room temperature, the immobilizates are rehydrated in a mineral salt medium (20 times more than required). The incubation of the cell-loaded gel substance is carried out in the same medium (40 times more than required) at 30 degrees Celsius. The medium is changed several times during the growing phase in order to provide the immobilized biomass with an adequate nutrient supply.

If 0.25 g of the immobilized bio-catalyst thus obtained are placed in 40 ml of mineral salt medium together with 24.4 g L-1 glycerine, within 3.25 h the concentration of 1.3-PD increases by 2.8 g L-1. This corresponds to a catalyst activity of 0.14 g 1.3-PD per g cat per hour. After deducting the activity of fully developed cells, the result is a catalyst activity of 0.08 g 1.3-PD (g_{cat} x h).

Example 4:

15.8 g of water is added to 2 g PVAL and 1.2 g polyethylene glycol (PEG 1000) and the process is continued according to Example 1.

After cooling the polymer suspension to approx. 30-37 degrees Celsius, 1 ml of a defined spore suspension of the fungus Aspergillus terreus is added to a polymer solution of 20 g and dispersed. The spore suspension is selected so that 5 d of fouling in the growth

medium results in a dry biomass load of 0.05 wt.%.

After 70 wt.% of the water has evaporated at room temperature, the immobilizates are rehydrated in a mineral salt medium for Aspergillus terreus (20 times more than required).

The incubation of the immobilizates is carried out in the growing medium. The growing medium is replaced with production medium for producing the itaconic acid.

Compared to the same amount of free fungus cells, the immobilizates thus produced have an initial activity of approx. 60% directly after immobilization. If 0.2 g of gel substance is incubated in 100 ml of production medium together with 60 g/l glucose, a productivity of 35 mg of itaconic acid (g_{cat} x h) is achieved after 7 d.

Example 5:
Larger amounts of gel substances are obtained by dripping the polymer solution (composition according to Example 1) through a system of multiple nozzles onto a conveyer belt. According to the principle of a belt dryer, the PVA drops are dehydrated in a tunnel drier to a defined residual moisture content and subsequently collected in a collection container by means of a scraper, where they are rehydrated and washed.

Example 6:
In the production process according to Example 1, the polymer solution is not dripped, but poured into prefabricated semi-open forms of optional length with an interior diameter of 1-10 mm.

After rehydration in water, the strands can be stretched to 3-4 times their length without breaking. This stretching is irreversible. A strand produced in this way can be loaded with a weight of 500 g without breaking.

Example 7:

After a storage period of 14 days, the strands produced according to Example 6 are mechanically characterized in tap water. At that time, the strands are approximately 8 mm wide and approximately 1 mm high. The degree of rehydration takes into account the strand's loss of weight after rehydration and 14 d storage in water in relation to the total mass of the polymer solution prior to the dehydration process. The strands have an elastic behaviour up to an elongation at tear of 40%.

- Mechanical characterization of the produced strands with various degrees of dehydration for the composition 10 wt.% PVA and 6 wt.% PEG 1000:

Residual water content after dehydration [%]	Degree of rehydration [%]	Elongation at tear [%]	E-modulus [N/mm^2]
27	76	455	0.11
20	74	420	0.11
15	68	410	0.18
13	65	390	0.24
10	63	380	0.27
1	57	360	0.34

- Mechanical characterization of the strands at a degree of dehydration of 80 wt.% for the composition 10 wt.% PVA and 8 wt.% PEG for various types of PEG:

Type of PEG	Degree of rehydration [%]	Elongation at tear [%]	E-modulus [N/mm^2]
400	57	410	0.27
600	66	290	0.22
800	82	360	0.19
1000	84	420	0.11
1350	92	370	0.12

- Mechanical characteristics of the PVA hydrogel strands for various concentrations of PVA with the addition of 6 wt.% PEG 1000 at a degree of dehydration (amount of water evaporated during the dehydration process) of 80 wt.%:

PVAL [%]	Elongation at tear [%]	E-modulus [N/mm^2]
8	350	0.09
10	420	0.11
12	420	0.17
14	460	0.19
16	440	0.25

- Mechanical characteristics of the strands at a degree of dehydration of 80 wt.% for the composition 10 wt.% PVA and 6 wt.% PEG 1000 for various rehydration media:

Rehydration medium	Elongation at tear [%]	E-modulus [N/mm^2]
Tap water	420	0.11
K_2HPO_4 (100 mmol/1)	410	0.17
K_2SO_4 (120 mmol/1)	530	0.15
$CaCl_2$ (120 mmol/1)	360	0.10
KCl (175 mmol/1)	370	0.15

Example 8:

Gel substances are produced according to Example 1 and rehydrated in deionized water (5 µS H_2O). The degree of rehydration for various degrees of dehydration of the gel substances is defined directly after the rehydration process. With a degree of rehydration of 100 wt.%, the weight of the gel substances prior to the dehydration process and after the rehydration process is the same, as shown in the attached drawing.

Claims

1. Process for producing a biocatalyst with a biologically active material, introduced into a gel of polyvinyl alcohol, in the form of microorganisms, enzymes, spores and/or cells with the process steps

   a) Use of an aqueous polyvinyl alcohol solution with a degree of hydrolysis of $\geq$ 98 mol %.

   b) The addition of an additive that is dissolved in the aqueous polyvinyl alcohol solution and forms a separate, finely distributed and aqueous phase after concentration of the solution.

   c) Addition of the biologically active material.

   d) Dehydration of the aqueous solution to a maximum residual water content of 50 wt.% in order to cause the phases to separate and hence the polyvinyl alcohol to gel.

   e) Rehydration of the polyvinyl alcohol in an aqueous medium.

2. Process according to Claim 1, in which the polyvinyl alcohol solution has a concentration of 4 - 30 wt.%, preferably 6 - 16 wt.%.

3. Process according to Claims 1 and 2, in which a water-soluble additive is used which has an affinity to water at least similar to that of the polyvinyl alcohol.

[Stamp:]
Revised sheet
IPEA/EP

4. Process according to Claims 1 to 3, in which the water-soluble additive is selected from the group cellulose esters, cellulose ethers, starch esters, starch ethers, polyalkylene glycol ethers, polyalkylene glycols, long-chain alkanoles ($n \geq 8$), sugar esters and sugar ethers.

5. Process according to Claim 4, in which polyethylene glycol is used as a water-soluble additive.

6. Process according to Claims 1 to 5, in which the water-soluble additive is used in a concentration of 4 - 20 wt.%, preferably 6 - 10 wt.%.

7. Process according to Claims 1 to 6, in which the dehydration of the aqueous solution is carried out until a residual water content of at least 10 wt.% is reached.

8. Process according to Claim 7, in which the dehydration of the aqueous solution is carried out until a residual water content of 10 - 30 wt.% is reached.

9. Process according to Claims 1 to 8, in which the dehydration process is carried out after dripping the solution onto a hard surface.

10. Process according to Claims 1 to 9, in which the dehydration process is carried out after pouring the solution into a form.

[Stamp:]
Revised sheet
IPEA/EP

11. Process according to Claims 9 and 10, in which the dripping or pouring is carried out in such a way that the gel substance is formed with a diameter at least double its height.

12. Process according to Claim 11, in which the dripping or pouring is carried out in such a way that the gel substance is formed with a diameter of > 1 mm, preferably between 2 and 4 mm, and a height between 0.1 and 1 mm, preferably between 0.2 and 0.4 mm.

13. Process according to Claims 1 to 8, in which the dehydration process is carried out after pouring the solution to form a long strand.

14. Process according to Claims 1 to 13, in which the dehydration process is carried out after pouring the solution onto a base material.

15. Process according to Claims 1 to 14, in which the rehydration is carried out in tap water.

16. Process according to Claims 1 to 14, in which the rehydration is carried out in a saline solution.

17. Process according to Claim 16, in which a culture solution for the biologically active material is used as the saline solution.

18. Process according to Claims 16 and 17 using a saline solution containing polyvalent anions.

[Stamp:]
Revised sheet
IPEA/EP

19. Process according to Claims 1 to 18, in which the dehydration process is completely carried out during the time the created drop falls in a drop tower.

20. Mechanically highly stable biocatalyst of polyvinyl alcohol, produced according to the process according to Claims 1 to 19.

21. Biocatalyst according to Claim 20, produced in a lenticular form in which the diameter is significantly greater than the height.

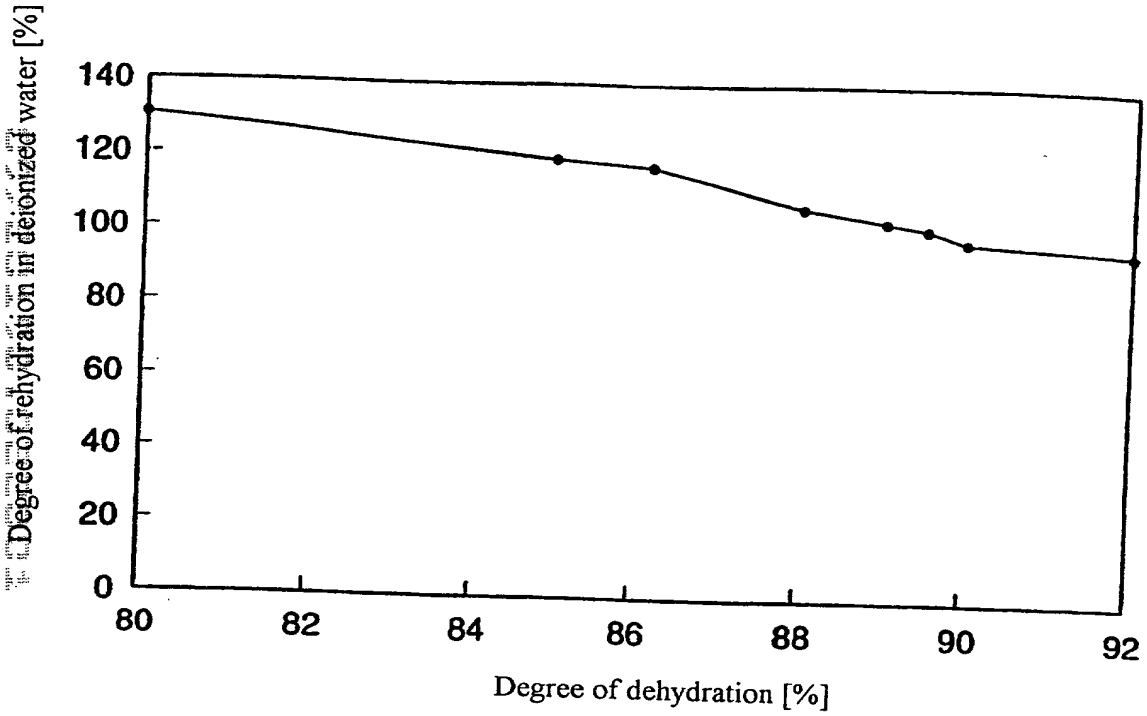
22. Biocatalyst according to Claims 20 and 21 with a magnetic additive.

23. Process for producing a product created by transformation with a biocatalyst according to Claims 20 to 22.

24. Process according to Claim 23 for producing 1.3-propane diol.

25. Process according to Claim 24 for producing itaconic acid.

[Stamp:]
Revised sheet
IPEA/EP


Degree of rehydration in deionized water [%]
140
120
100
80
60
40
20
0
80
82
84
86
88
90
92
Degree of dehydration [%]

[Graph:]

[Vertically:]

Degree of rehydration in deionized water [%]

[Horizontally:]

Degree of dehydration [%]

27/12

DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

We, Dr. Klaus-Dieter Vorlop, residing in Braunschweig, Germany, and Maren Jekel, residing in Duesseldorf, Germany, declare that we are citizens of Germany and that we believe we are the original and first inventors of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Process for Producing a Polyvinyl Alcohol Gel and a Mechanically Highly Stable Gel Produced Thereby

the specification of which is attached hereto.

We hereby state that we have reviewed and understand the contents of the above identified specification, including the claims.

We acknowledge the duty to disclose to the Patent and Trademark Office all information known to be material to patentability as defined in §1.56.

We hereby claim foreign priority benefits under Title 35, United States Code, §119 of **PCT Application No. PCT/DE99/00975, filed 30 March 1999, and which named the United States as a designated country.**

There is no foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

We hereby appoint Robert E. Muir, Patent Office Reg. No. 23,017, Kevin M. Kercher, Patent Office Reg. No. 33,408, Richard J. Musgrave, Patent Office Reg. No. 44,960, telephone number 309-637-4900, and H. Frederick Rusche, Patent Office Reg. No. 45,061, telephone number 314-421-4800, my attorneys and/or agents, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected with this application. Please address all correspondence to:

Robert E. Muir
Husch & Eppenberger, LLC
401 Main Street, Suite 1400
Peoria, Illinois 61602-1241

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Klaus-Dieter Vorlop — 19.12.2000

Dr. Klaus-Dieter Vorlop — Date
Hochstrasse 7
D-38102 Braunschweig, Germany DEX

::ODMA\PCDOCS\PEORIA\100375\1

DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

We, Dr. Klaus-Dieter Vorlop, residing in Braunschweig, Germany, and Maren Jekel, residing in Duesseldorf, Germany, declare that we are citizens of Germany and that we believe we are the original and first inventors of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Process for Producing a Polyvinyl Alcohol Gel and a Mechanically Highly Stable Gel Produced Thereby

the specification of which is attached hereto.

We hereby state that we have reviewed and understand the contents of the above identified specification, including the claims.

We acknowledge the duty to disclose to the Patent and Trademark Office all information known to be material to patentability as defined in §1.56.

We hereby claim foreign priority benefits under Title 35, United States Code, §119 of **PCT Application No. PCT/DE99/00975, filed 30 March 1999, and which named the United States as a designated country.**

There is no foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

We hereby appoint Robert E. Muir, Patent Office Reg. No. 23,017, Kevin M. Kercher, Patent Office Reg. No. 33,408, Richard J. Musgrave, Patent Office Reg. No. 44,960, telephone number 309-637-4900, and H. Frederick Rusche, Patent Office Reg. No. 45,061, telephone number 314-421-4800, my attorneys and/or agents, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected with this application. Please address all correspondence to:

Robert E. Muir
Husch & Eppenberger, LLC
401 Main Street, Suite 1400
Peoria, Illinois 61602-1241

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

_____ _____
Dr. Klaus-Dieter Vorlop Date
Hochstrasse 7
D-38102 Braunschweig, Germany

2.00

Maren Jekel

Date 20/12/00

Maren Jekel
Benkstrasse 79
D-40476 Duesseldorf, Germany

DEX